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Adult respiratory distress syndrome due to *Chlamydia pneumoniae* in a young adult

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A case of life-threatening *Chlamydia TWAR pneumonia* complicated by encephalitis in a young, previously healthy adult is described. The patient presented with full blown adult respiratory distress syndrome and required prolonged ventilatory support and rigorous antibiotic and supportive care. He recovered fully without any neurologic sequelae. *Chlamydia pneumoniae* pneumonia should be included in the differential diagnosis of the severe community acquired pneumonia, because if properly sought and adequately treated, may have an excellent outcome.

Introduction

About 10% of pneumonia cases admitted to hospital have been shown to be associated with TWAR infection, and of these 70–90% are mild with short-term disability. If these are not treated, there may be prolonged symptoms with malaise and cough extending for several months, but a serious life-threatening illness in a normal young host has not been described to date. Although severe episodes and even deaths have been reported in patients with pre-existing severe chronic diseases (1) and in the elderly (2), no cases of severe pneumonia in normal hosts due to TWAR have been reported. Attempts to diagnose this pathogen have been rarely, if ever, performed (3).

This report describes a case of severe *Chlamydia pneumoniae* community-acquired pneumonia with adult respiratory distress syndrome. A simple diagnostic methodology that is useful in the everyday clinical practice is also described.

Case Report

A 42-year-old man of previous good health was admitted to the emergency room in acute respiratory distress. A week previously, he had suffered a common cold-like illness with headaches, malaise, and generalized weakness, without fever. For the previous 4 days, he had experienced high fever (39°C) with chills, sweats and diarrhoea (6 in 24 h). Physical examination revealed an ill-appearing, febrile, markedly tachypnoeic man with tachycardia, normal blood pressure and a few crackles over the right upper and left lower lung fields. He appeared confused, disoriented, with seriously diminished mental status, and had bouts of grand mal seizures, due to probable encephalitis. Arterial blood gas determination with an FiO_2 of 0·5 was compatible with acute hypoxaemic respiratory failure (PaO_2 48 mmHg, $PaCO_2$ 40 mmHg, pH 7·32), so he was intubated receiving controlled mechanical ventilation with 100% O_2, tidal volume of 10 ml kg^{-1} and 10 cm H_2O PEEP on the first day. The patient had a severe acute lung injury (lung injury score of 10) and he fulfilled the criteria of its expanded definition (4); namely he had an associated clinical disorder (pneumonia) and a non-pulmonary organ failure (encephalitis). Chest X-ray revealed a dense right upper lobe infiltrate with concomitant fluffy nodular opacities scattered throughout both lung fields.

Laboratory studies demonstrated a haemoglobin level of 14·5 g dl^{-1}, haematocrit of 44%, white blood cell count of 7300 cells mm^{-3}, with 89% neutrophils, 8% lymphocytes and 2% monocytes. The erythrocyte sedimentation rate was elevated to 67 mm h^{-1}. Aspartase aminotransferase (ASAT) was 245 IU l^{-1}, alanine aminotranferase (ALAT) 69 IU l^{-1}, gamma glutamyltranferase (γGT) 92 IU l^{-1} and lactic dehydrogenase (LDH) 1060 IU l^{-1}. Renal biology and serum Na^+ were normal. He was put on empirical treatment proposed for severe community-acquired pneumonia (5) including erythromycin 4 g i.v. along with cefotaxime 8 g i.v. daily, that was changed to

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oral doxycycline for an additional 10-day period after diagnosis and clinical improvement. The patient required prolonged ventilatory support for the next few days, gradually improving and was successfully weaned on the 12th hospital day. He made a complete recovery with no neurologic sequelae.

Quantitative brush-protected-specimen cultures were non-diagnostic (sterile) for the presence of pathogenic bacteria, as well as blood cultures. Acute phase serum samples obtained on the 12th day of illness, showed an IgM antibody titer >1/80 (normal 0–1/16) by indirect immunofluorescence (Bios, Germany) directed against the major outer membrane protein, of *C. pneumonia* being genus specific, while at the same time indirect immunofluorescence against *Chlamydia psittaci* was negative. The patient had a negative rheumatoid factor, so false positive reactions were excluded (broadly reactive IgM activities to all three chlamydial species were frequently the result of the presence of rheumatoid factor in the test sera). *Chlamydia pneumoniae* were identified concomitantly in nasopharyngeal swab specimen with *C. pneumoniae* specific monoclonal antibody, unconjugated (Cellabs, Australia). Acute and convalescent complement fixing antibodies were negative for *Influenza A* and *B, Mycoplasma pneumoniae, Parainfluenza* type 1 and 3, *Coxiella burnetti,* and *Chlamydia psittaci* (titer <1/80. Indirect immunofluorescence was negative for *Legionella pneumophila,* serotypes 1–6 (Viron, Switzerland). The patient denied any contact with birds by recreational or occupational exposure, and he had no history of recent urethritis.

Discussion

Chlamydia pneumoniae is now considered the third species of Chlamydia causing human disease, the other two being *C. trachomatis* and *C. psittaci.* There are two known serovariants, namely TWAR and IOL-207, of which TWAR is best understood. The serological profile of the present patient is indicative of an acute infection rather than a re-infection, because IgM antibodies at re-infection may not appear or exist at low titers (6). Re-infection appears to be generally, although not always, associated with milder illness than a first infection. A high antibody titer as early as the 12th day of hospital stay (19th day of illness) is not unusual (7) and may in fact represent an index of clinical severity. Severe life-threatening pneumonia due to Chlamydia TWAR has been described by Marrie *et al.*, where in their series, four patients were mechanically ventilated and two died, but the hosts were old with severe comorbidity (1).

The therapeutic regimen contained an erythromycin plus a third generation cephalosporin, because the authors wanted a broad spectrum antibiotic coverage in such a serious condition. Furthermore it is also known that copathogens are usually present along with Chlamydia TWAR (8). Even though the initial presentation was suggestive of Legionella infection, this seemed unlikely later in view of the serological and electrolytic profiles. Although mental status changes can occur after severe hypoxaemia, the combination of seizures with the former is suggestive of encephalitis. Central nervous system manifestations are not unusual with *C. pneumoniae* infections and in one study (9), 38% of patients showed mental status changes. *Chlamydia pneumoniae* like *Mycoplasma pneumoniae* may be complicated by extrapulmonary manifestations as in the present case, and so far erythema nodosum, thyroiditis, encephalitis and the Guillain-Barré syndrome have been described. These have been attributed to the 60 kDa protein of *C. pneumoniae*, which is a delayed-type hypersensitivity antigen (8). The chest X-ray appearance showing a lobar distribution found predominantly in bacterial pneumonias confirms previous findings that there are not clinical, radiographic or laboratory features characteristic of atypical bacterial infection in hospitalized patients.

The microimmunofluorescence test using *C. pneumoniae* specific antigen (TW-183) is considered the gold standard for diagnosis, but it is restricted to reference and research laboratories and is not commercially available. Furthermore, it has been shown recently in some studies to have cross-reactions with the other Chlamydia species, so there is a need for a more objective and more accurate test for serodiagnosis, because it is inadequate (10). The combination of high genus specific antibody titer along with the negative serology for *C. psittaci* and the direct identification of Chlamydia TWAR in nasopharyngeal swabs established the diagnosis. Although asymptomatic carriage in the nasopharynx from a previous infection is a rare possibility, this seems unlikely considering the serological profile of the present patient. Furthermore, history and the relative rarity of *C. psittaci* pneumonia strongly indicted the diagnosis. On the other hand, molecular techniques are now becoming available, but they need to be validated in terms of sensitivity and specificity. Culture of this fastidious organism is considered the gold standard for diagnosis, but requires some time (3 days), may suffer in terms of sensitivity, and needs expertise and equipment found only in specialized

laboratories. The authors think the simple diagnostic procedure used in this report can be useful in everyday practice for an initial identification of *C. pneumoniae* infection.

In conclusion, the above case illustrates that *C. pneumoniae* can be a cause of severe illness in healthy adults and should be included in the differential diagnosis of severe pneumonia.

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